IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE: DIET DRUGS (PHENTERMINE/ FENFLURAMINE/ DEXFENFLURAMINE) PRODUCTS LIABILITY LITIGATION	MDL DOCKET NO. 1203
	CIVIL ACTION NO. 2:11-cv-20001-HB
This document relates to: JAMIE D. CHEEK, Plaintiff, v. WYETH, formerly known as American Home Products Corporation et al., Defendants.	PLAINTIFF CHEEK'S RESPONSE IN OPPOSITION TO DEFENDANT WYETH'S MOTION TO EXCLUDE EXPERT TESTIMONY AND ENJOIN PLAINTIFF CHEEK'S CASE PURSUANT TO PRETRIAL ORDER NO. 2383

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I. INTRODUCTION

Plaintiff Jamie Cheek respectfully submits this memorandum in opposition to Defendant Wyeth's Motion to Exclude Plaintiff's Experts' Testimony and to Enjoin Pursuant to Pretrial Order No. 2383. Specifically, Wyeth has moved to exclude the testimony on the causation of Ms. Cheek's pulmonary arterial hypertension ("PAH")[1]

[1] Previous medical terminology only distinguished between primary pulmonary hypertension ("PPH") (of an unknown etiology) and secondary pulmonary hypertension (of a known etiology). Due to confusion regarding these classifications, the terminology has evolved to include multiple categories of pulmonary hypertension. One such category is pulmonary arterial hypertension ("PAH"), which has been subcategorized as either idiopathic pulmonary arterial hypertension ("IPAH"), which is PAH of an unknown etiology, or simply PAH, which indicates a known etiology. Plaintiff's Response employs the most current classification terminology.

proffered by her experts, Dr. Stuart Rich and Dr. Lewis Rubin ("Drs. Rich and Rubin"), for failing to satisfy the reliability requirement for admissibility set forth in *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579 (1993). Wyeth also seeks to enjoin Cheek from pursuing her claim based on its interpretation of the National Settlement Agreement (hereinafter "NSA").

Wyeth's motion must be denied. Dr. Rich's and Dr. Rubin's opinions and testimonies wholly satisfy the requirements for admissibility of expert testimony as set forth in the Federal Rules of Evidence and the *Daubert* standard. Furthermore, Dr. Rich's expert testimony has previously cleared the *Daubert* hurdle in a virtually identical case against Wyeth. *See Smith v. Wyeth-Ayerst Labs. Co.*, 278 F. Supp. 2d 684 (W.D.N.C. 2003). However, Wyeth, while pointing to no new evidence or methodology, seeks to re-litigate this issue based on its same untenable arguments in an attempt to get a favorable result this time around.

Wyeth's argument is flawed as it attacks individual pieces of evidence considered by Cheek's experts rather than considering the totality of evidence. Dr. Rich's and Dr. Rubin's testimony are derived from reliable evidence and sound methodology. Importantly, they have considered and interpreted the same studies as those relied on by Wyeth's experts. In fact, the study that is the foundation of Wyeth's epidemiology expert Dr. Mitchell Levine's testimony was designed by and participated in by Cheek's experts. This Court should deny Wyeth's motion as all of Wyeth's challenges are more properly considered, at best, challenges to the weight that should be given to Cheek's experts' testimony and thus, are simply arguments Wyeth should reserve for the trier of fact.

II. FACTUAL BACKGROUND

A. Plaintiff Jamie Cheek

Before delving into an analysis of the expert testimony of Drs. Rich and Rubin, a background of Ms. Cheek and her condition will be helpful. Cheek ingested diet drugs for approximately one month in 1991 and for over twelve months during 1995 to 1997.[2] In December 2007, she experienced severe shortness of breath, even with minimal activity, at which point an echocardiogram evidenced right atrial and right ventricular enlargement with pulmonary hypertension.[3] In February 2008, Ms. Cheek sought emergency treatment due to a near-syncopal episode and extreme shortness of breath with minimal activity.[4] On February 19, 2008, she was advised by her cardiologist, Dr. Gregory May, that he suspected PAH and referred her to the Medical University of South Carolina.[5] Finally, in May 2008, her diagnosis of diet-drug-induced PAH was confirmed based on results from her right heart catheterization. Additional testing ruled out diseases commonly associated with PAH, including any interstitial lung or thromboembolic disease.[6] Her treating physician, Dr. Kristin Highland, a Board-Certified pulmonologist, diagnosed Ms. Cheek with advanced PPH attributable to diet drug use.[7]

B. Pulmonary Arterial Hypertension

Pulmonary arterial hypertension is high blood pressure in the arteries of the lungs. In a patient with pulmonary hypertension, pressure builds in the arteries of the lungs because those arteries cannot carry as much blood due to narrowing, and, as a result,

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[2] Plaintiff's Medical Records from Dr. Harry Allen (hereinafter "Allen") (Exhibit "A" hereto), pp. 225-228, 231, 242, 249.
[3] *Id.* at 26-28.
[4] *Id.* at 13.
[5] *Id.* at 2-3, 6.
[6] *Infra.*, pp. 39-41.
[7] Plaintiff's Medical Records from the Medical University of South Carolina (hereinafter "MUSC") (Exhibit "B" hereto), pp. 20-23.

"[t]he heart needs to work harder to force the blood through the vessels against this pressure. Over time, this causes the right side of the heart to become larger."[8] Unlike PAH that is associated with other diseases, which can be treated, at least in part, by treating the underlying disease that contributes to the PAH, the prognosis for diet-drug-induced PAH is irreversible and typically fatal.[9]

Pulmonary arterial hypertension with no known cause (IPAH) is an extremely rare disease "with an estimated incidence of approximately 2 cases per million population. The diagnosis is essentially one of exclusion and often is made in its advanced stages because of the nonspecific nature of the early symptoms and signs of this condition."[10] PAH is characterized by a mean pulmonary artery systolic pressure greater than 25 mmHg at rest and a pulmonary artery occlusion pressure less than 15 mmHg, which cannot be ascertained without a right heart catheterization.[11] The current standard for diagnosing the specific form of PAH exhibited by the patient is performance of a differential diagnosis. A differential diagnosis uses the process of elimination to rule out possible factors that may have caused or contributed to a patient's PAH.

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[8] *See* "Pulmonary hypertension," A.D.A.M. Medical Encyclopedia, *available at http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001171/* (last visited Aug. 6, 2012).

[9] Xing-Guo Sun et al., *Exercise Pathophysiology in Patients With Primary Pulmonary Hypertension*, 104 CIRCULATION 4, 429, 429 (2001) (Exhibit "C" hereto).

[10] Eduardo Bossone et al., *Echocardiographic Features of Primary Pulmonary Hypertension*, 12 J. AM. SOC. ECHOCARDIOGR. 8, 655-662, 655 (1999) (Exhibit "D" hereto) (footnotes omitted) (referencing the following sources: (1) S. Rich, E. Braunwald, & W. Grossman, "Pulmonary Hypertension." In: *Heart Disease: A Textbook of Cardiovascular Medicine*, 780-806 (E. Braunwald, ed., 5th ed. 1997); (2) L. J. Rubin, *Primary Pulmonary Hypertension*, 336 N. ENGL. J. MED. 11, 7 (1997); (3) L. J. Rubin, *ACCP Consensus Statement: Primary Pulmonary Hypertension*, 993 CHEST 104, 236-49 (1993); (4) L. Abenhaim et al., *The International Primary Pulmonary Hypertension Study*, 105 CHEST 92, 37S-41S (1994) (Exhibit "E" hereto); (5) *Primary Pulmonary Hypertension: Report on a WHO Meeting*, Geneva: World Health Organization, 7-45 (S. Hatano & T. Strasser, eds., 1975); and (6) S. Rich et al., *Primary Pulmonary Hypertension: A National Prospective Study*, 107 ANN. INTERN. MED. 216-223 (1987)).

[11] R. Souza et al., *Pulmonary Arterial Hypertension Associated With Fenfluramine Exposure: Report of 109 Cases*, 31 EUR. RESPIR. J. 2, 343, 344 (2008) (Exhibit "F" hereto); Champion Dep. 63:24-64:11, June 27, 2012 (Exhibit "G" hereto) (stating that he could never diagnose PAH without a right heart catheterization).

According to the most recent classification standards agreed upon by an international group of pulmonary experts during the "Fourth World Symposium on Pulmonary Arterial Hypertension" held in Dana Point, California, in 2008, there are four sub-classifications of PAH in adults: idiopathic, heritable, drug- and toxin-induced, and PAH associated with other diseases.[12] Pulmonary arterial hypertension associated with other diseases can result from connective tissue diseases, HIV infection, portal hypertension, congenital heart diseases, schistosomiasis, or chronic hemolytic anemia. *See id.* at S45 (Table 2). Thus, a complete medical history and considerable testing must be completed in order to rule out potential causes of PAH and establish which sub-classification of PAH is an appropriate diagnosis. It is only when all other known risk factors of PAH are eliminated that a diagnosis of IPAH would be suitable because "[i]diopathic PAH corresponds to sporadic disease in which there is neither a family history of PAH *nor an identified risk factor*." *Id.* at S44 (emphasis added).

The Dana Point classification expressly identifies multiple risk factors within the sub-classification group of drug- and toxin-induced PAH and describes them as "'any factor or condition that is suspected to play a predisposing or facilitating role in the development of the disease....'" *Id.* at S45 (unattributed quotation in original). These "risk factors were categorized as definite, very likely, possible, or unlikely, based on the 'strength of their association with PH and their probable causal role.'" *Id.* (unattributed quotation in original). The label of a "definite" risk factor was attributed to those drugs and/or toxins that had been linked with an epidemic of pulmonary hypertension or had been the subject of "large, multicenter epidemiologic studies demonstrating an

[12] G. Simonneau et al., *Updated Clinical Classification of Pulmonary Hypertension*, 54 J. AM. COLL. CARDIOL. S43, S45 (2009) (Exhibit "H" hereto).

association between a drug and PAH." *Id.* Fenfluramine and dexfenfluramine are two of only four drugs/toxins identified as "definite" risk factors of PAH.[13]

In reaching this conclusion, the attendees at the "Fourth World Symposium on Pulmonary Arterial Hypertension" relied, in part, on two of the very same sources used by Drs. Rich and Rubin in drawing their conclusions that Ms. Cheek's use of diet drugs caused her PAH. [14] The analysis performed by Dr. Souza of over one-hundred cases of PAH was interpreted by the Dana Point classification as "suggesting that fenfluramine exposure represents a potential trigger for PAH...." G. Simonneau at S45. Likewise, Dana Point concludes that the Surveillance of Pulmonary Hypertension in America (hereinafter "SOPHIA") Study "confirmed the association of fenfluramine and dexfenfluramine intake with the development of PAH." *Id.* at S45.

C. Cheek's Experts and Their Testimony

The experience, education, and qualifications of Cheek's experts, Dr. Stuart Rich and Dr. Lewis Rubin, as to the medical field of pulmonary hypertension ("PH") have not been called into question. Therefore, it is unnecessary to exhaustively detail the achievements of Drs. Rich and Rubin, but a brief summary of their credentials and testimony provides a helpful context.

Dr. Rich is one of the foremost experts in the world on PAH. He has written numerous peer-reviewed publications, many of which involve PAH, that have been cited to by numerous other works.[15] As for the relationship between PAH and fenfluramines,

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[13] *Id.* at S45 (Table 3).

[14] Souza, *supra* note 11; A. Walker et al., *Temporal Trends and Drug Exposures in Pulmonary Hypertension: an American Experience*, 152 AM. HEART J. 521-526 (2006) (Exhibit "I" hereto).

[15] For articles authored or co-authored by Drs. Rich and Rubin, see their respective *curricula vitae* attached hereto as Exhibits J and K. Examples of articles citing to the work of Dr. Stuart Rich and/or Dr. Lewis Rubin include, but are not limited to: Souza, *supra* note 11; Simonneau, *supra* note 12; and Bossone, *supra* note 10.

Dr. Rich was a principal investigator and co-author of the 1994 International Primary Pulmonary Hypertension Study (hereinafter "IPPHS"),[16] a lead author of Surveillance of North American Pulmonary Hypertension (hereinafter "SNAPH"),[17] and has been qualified to and testified on specific causation of PAH in several suits involving diet drugs produced by Wyeth. *See* Exhibit J; *see, e.g.*, *Smith v. Wyeth-Ayerst Labs. Co.*, 278 F. Supp. 2d 684 (W.D.N.C. 2003); *Linnen v. A.H. Robins Co., Inc.*, No. 972307, 2000 WL 145758 (Mass. Super. Jan. 4, 2000) (holding that Dr. Rich's PAH-causation testimony was both relevant and reliable). Furthermore, Dr. Rich's clinical practice focuses almost primarily on the diagnosis and treatment of PAH.

Dr. Rubin's experience and credentials are equally impressive. Dr. Rubin has spent most of his life as a clinician and professor of cardiopulmonology. *See* Exhibit K. In addition to being on the expert panel for IPPHS, Dr. Rubin has written numerous peer-reviewed publications, of which several deal with PAH. *See* Exhibit K. Currently, Dr. Rubin serves as a consultant for drug development, interpretation of data, and submission to regulatory authorities for several major drug companies including Defendant Pfizer. *See* Rubin Dep. 9:15-11:9, June 20, 2012 (Exhibit "N" hereto).

In Cheek's case, Drs. Rich and Rubin have testified to a degree of reasonable medical certainty that her exposure to Wyeth's diet drugs caused her to develop PAH. The experts' testimony and opinions are based upon their review of Cheek's medical

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[16] IPPHS was an epidemiologic study that conclusively determined the existence of a strong association between Wyeth's diet drugs and PAH. When applied to the three Bradford Hill factors, this study established undisputed evidence of a causal link between the drugs and PAH. Abenhaim, *supra* note 10; Lucien Abenhaim et al., *Appetite-Suppressant Drugs and the Risk of Primary Pulmonary Hypertension*, 335 N. ENGL. J. MED. 9, 609-616 (1996) (Exhibit "L" hereto).

[17] Stuart Rich, Lewis Rubin, et al., *Anorexigens and Pulmonary Hypertension in the United States: Results From the Surveillance of North American Pulmonary Hypertension*, 117 CHEST 3, 870-874 (2000) (Exhibit "M" hereto). SNAPH studied cases of PAH across North America, and it supported the causal link between diet drugs and PAH as well as provided additional evidence of a longer latent period.

records, all relevant peer-reviewed publications and studies, and their own professional clinical experience and observations. *See* Rubin Dep.14:17-15:7, 25:9-26:8, June 20, 2012. Their testimony is not rooted in a single piece of evidence but is based on a consideration of the entirety of available evidence.

III. THE COURT SHOULD TAKE JUDICIAL NOTICE OF THE RELIABILITY OF CHEEK'S EXPERTS' TESTIMONY BASED ON A PRIOR ADJUDICATION IDENTICAL TO THE CASE AT BAR OR, IN THE ALTERNATIVE, FIND IT PERSUASIVE TO RULING IN FAVOR OF ADMISSIBILITY.

While Wyeth only deems it worthy of dismissive mention in a footnote, the district court's decision in *Smith v. Wyeth-Ayerst Labs. Co.*, 278 F. Supp. 2d 684 (W.D.N.C. 2003), is highly relevant to the instant motion and supports, if not requires, the admissibility of Cheek's experts' testimony. *Smith* meticulously addressed the same reliability issues raised by Wyeth's motion and provides a clear explanation for admissibility equally applicable to the facts of Cheek's case. As will be further discussed below, Cheek's experts' testimony satisfies the principles of *Daubert* and is admissible. However, this Court, in the interest of judicial economy, should take judicial notice of the reliability of the experts' testimony to swiftly dispose of Wyeth's meritless motion or, in the alternative, view it as relevant evidence supportive of admissibility.

A. Overview of *Smith v. Wyeth-Ayerst*

Plaintiff in *Smith* was diagnosed with pulmonary hypertension in 2001, four years after she had last ingested Wyeth's drugs Pondimin and Phentermine. *Id.* at 689-690. She took the diet drugs for a total of eight and one-half months. *Id.* at 689. Dr. Stuart Rich was Plaintiff's primary expert witness, and his differential diagnosis of Plaintiff concluded that her pulmonary hypertension was caused by Wyeth's diet drugs. *Id.* at

692. Wyeth moved to exclude Dr. Rich's testimony based on arguments identical to those presented by Defendant in the instant case. First, Wyeth argued that IPPHS did not fit the facts of Plaintiff's case and was not reliable evidence. *See id.* at 691-695. Second, Dr. Rich's differential diagnosis was challenged for not considering idiopathic PAH as a potential cause, its reliance being based on IPPHS, and Plaintiff expert's use of case reports. *See id.* at 695-697.

Regarding IPPHS, the court determined that "IPPHS did not conclude there is no risk beyond (12) months of the last use.... [I]t defies logic to contend that the risk existed at day 364, but not at day 366." *Id.* at 694. The court acknowledged that exactly how long the increased risk continues is unknown, but the "unknown does not render the Plaintiff's proffered opinions unreliable." *Id.* at 695. Although the court agreed that IPPHS was not powered to address latency issues, it still held that IPPHS was reliable, scientific evidence to support Plaintiff's theory of causation. The court arrived at its conclusion notwithstanding the fact that the study did not directly address latency. *Id.* The Court concluded that case reports could provide supportive data and be relied upon in conjunction with other medical literature. *See id.* The Court also held that Dr. Rich's differential diagnosis was admissible under *Daubert* and "the existence of idiopathic PPH doesn't render Dr. Rich's opinion inadmissible, but instead goes to the weight of the evidence." *Id.* at 692.

B. This Court Should Take Judicial Notice of Reliability

In *Pritchard v. Dow Agro Sciences*, the District Court for the Western District of Pennsylvania stated that the Third Circuit recognizes "that '[t]he reliability of expert testimony founded on reasoning from epidemiological data is generally a fit subject for

judicial notice; epidemiology is a well-established branch of science and medicine, and epidemiological evidence has been accepted in numerous cases.'" *Pritchard v. Dow Agro Scis.*, 705 F. Supp. 2d 471, 484 (W.D. Pa. 2010) *aff'd*, 430 F. App'x 102 (3d Cir. 2011) *cert. denied*, 132 S. Ct. 508 (U.S. 2011) (quoting *DeLuca v. Merrell Dow Pharmaceuticals, Inc.*, 911 F.2d 941, 954 (3d Cir. 1990)). While the opportunity to invoke this principle does not often arise, the facts of this case justify its application.

Cheek's experts' testimony is grounded in the IPPHS epidemiological study, numerous peer-reviewed journal case reports, and the vast clinical experience of the experts themselves. Thus, her experts' testimony has an even stronger foundation than that based solely on epidemiological data. Furthermore, by way of *Smith*, Dr. Rich's methodology was challenged by Wyeth previously on precisely the same basis as it now challenges Cheek's experts' testimony. Dr. Rich's testimony was determined to be reliable after a two-day evidentiary hearing. A decision by the Court to take judicial notice would not unfairly prejudice Wyeth as it has previously had a full and fair opportunity to litigate the question, and it would not be precluded from cross-examining the experts at trial. While Wyeth will likely rebuke this assertion and claim that the latent period is different, the reliability of the experts' methodology does not change with a longer latent period as they are both outside the exact confines of one-year after cessation, which IPPHS was powered to study.

Even if the Court were to conclude that it is improper in this instance to apply judicial notice to Cheek's experts' entire testimony, this Court should still, at a minimum, take judicial notice of the reliability of IPPHS as it undisputedly established an association and causation between diet drugs and PAH. The general causation issue does

not change from plaintiff to plaintiff as long as each plaintiff establishes that he or she consumed the drug.

C. The *Smith* Case is Relevant Evidence that Supports Reliability

Even if this Court finds that judicial notice is an improper means of disposing of Wyeth's baseless arguments, the Court should still view *Smith* as persuasive evidence of the reliability of Cheek experts' testimony in conjunction with the *Daubert* analysis below. The opinion in *Smith* reads as though it were a response to Wyeth's motion in the instant case. In *Smith*, Wyeth also focused on the latency aspect of causation as being unsupported by evidence. While Cheek's latency period is longer than that of the plaintiff in *Smith*, this difference should not discredit the methodology of her experts, and the evidence relied on by Drs. Rich and Rubin has only grown stronger since the court's opinion in *Smith*. *See infra* pp. 16-17. It should be noted that Cheek was exposed to diet drugs for a longer period of time than the plaintiff in *Smith*. *See supra* p. 3. At most, Wyeth's arguments go to the weight that should be given to Dr. Rubin's and Dr. Rich's testimony.

Wyeth aims to rehash these issues in an attempt to overcome the precedent set in *Smith* and "stop the bleeding" that has resulted from their dangerous product. But as the Supreme Court has eloquently stated, "Judicial precedents are presumptively correct and valuable to the legal community as a whole. They are not merely the property of private litigants and should stand unless a court concludes that public interest would be served by a vacatur." *U.S. Bancorp Mortg. Co. v. Bonner Mall P'ship*, 513 U.S. 18, 26 (1994) (quoting *Izumi Seimitsu Kogyo Kabushiki Kaisha v. U.S. Philips Corp.*, 510 U.S. 27, 40 (1993) (Stevens, J., dissenting)). While the issue at hand does not involve precedents in

the traditional sense, the same underlying principles should apply in order to keep Wyeth from re-litigating this issue over and over.

Smith addressed the issues that Wyeth has raised with regard to Cheek's experts' reliance on IPPHS, case reports, and differential diagnosis under the *Daubert* standard. While Dr. Rubin was not an expert in *Smith*, his methodology, testimony and differential diagnosis are based on the same evidence as Dr. Rich's in that case and in the case at bar. Therefore, the court should find *Smith* equally persuasive as to the reliability of Dr. Rubin's testimony.

Wyeth's motion improperly dwells on the *conclusions* that result from the experts' methodology and on the fact that there is no case-controlled epidemiologic study of latency *per se* rather than focusing, as the law requires, on the methodology itself. As noted in *Smith*, most courts agree that an epidemiological study does not have to be available that "squarely address[es]" the causation issue that is before the court. *Smith,* 278 F. Supp. 2d at 694. The parallel facts and issues presented in *Smith* should allow a quick conclusion on the issues of reliability presented in Wyeth's motion. As one District Court in the Third Circuit has remarked, "the decision of other courts presented with similar questions are clearly relevant to the inquiry [of reliability and admissibility]." *United States v. Ewell*, 252 F. Supp. 2d 104, 111 n.11 (D.N.J. 2003).

* * *

Cheek respectfully requests that this Court take judicial notice of the reliability of her experts' testimony and the evidence upon which it is based. Wyeth's motion is obviously an attempt to take a "second bite of the proverbial apple," but its argument has not gained any stature since its last attempt to exclude Dr. Rich's testimony. If this Court

determines that judicial notice is not the appropriate manner to resolve Wyeth's motion, the Court should nonetheless view *Smith* as persuasive in regards to the reliability of Cheek's experts' testimony and underlying methodology. Cheek's case and *Smith* are nearly identical. Both cases involve the same Defendant, drugs, disease, and also share one expert. Although the latency period before the onset of PAH differs in these two cases, the evidence on which Wyeth itself relies – the IPPHS assessment of "past users" – is exactly the same in both cases. This fact makes this Court's adoption of the court's holding in *Smith* all the more appropriate.

The persuasive evidence provided by *Smith*, when combined with the other evidence relied upon by Cheek's experts, clearly satisfies the liberal and flexible *Daubert* standard. Because the evidence so clearly supports admissibility, this Court should exercise its discretionary authority to avoid an unnecessary reliability hearing in this ordinary case "where the reliability of [the] expert[s'] methods [are] properly taken for granted." *Kumho Tire Co., Ltd. v. Carmichael*, 526 U.S. 137, 152 (1999). This will avoid "unjustifiable expense and delay" and serves the interest of judicial economy. *Id.* at 152 (quoting F. R. Evid. 102).

IV. CHEEK'S EXPERTS' TESTIMONY IS ADMISSIBLE BECAUSE THEIR TESTIMONY SATISFIES THE RELIABILITY REQUIREMENTS SET FORTH BY *DAUBERT* AND THIRD CIRCUIT CASE LAW.

Even without a consideration of the highly relevant *Smith* decision, this Court should find that the expert opinions of Dr. Rubin and Dr. Rich satisfy the requirements set forth by the Supreme Court in *Daubert* and expounded upon in subsequent Third Circuit case law. The admissibility of their testimony is best made clear by viewing Cheek's experts' methodology and the evidence they relied on in the context of the

Daubert guideposts and additional relevant factors from *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717 (3d Cir. 1994) (hereinafter "*Paoli*").

A. LEGAL STANDARD

Rule 702, Fed. R. Evid., which governs the admissibility of expert testimony, requires the consideration of the following four factors when determining admissibility:

> (a) the expert's...knowledge will help the trier of fact to understand the evidence or to determine a fact in issue; (b) the testimony is based on sufficient facts or data; (c) the testimony is the product of reliable principles and methods; and (d) the expert has reliably applied the principles and methods to the facts of the case.

The Federal Rules of Evidence embody a strong preference for admitting any evidence that may assist the trier of fact. *See* Fed R. Evid. 401. Rule 702, which governs the admissibility of expert testimony, has a "liberal policy of admissibility." *Pineda v. Ford Motor Co.*, 520 F.3d 237, 244 (3d Cir. 2008). As the Supreme Court held in *Daubert*, "[u]nlike an ordinary witness...an expert is permitted wide latitude to offer opinions." *Daubert*, 509 U.S. at 592 (citing Fed. R. Evid. 702 and 703).

In *Daubert*, the Supreme Court clarified that Fed. R. Evid. 702 speaks to the relevance and reliability of the proposed expert testimony. Since the relevancy of the expert testimony proffered by Drs. Rich and Rubin has not been challenged, the primary issue before the Court is the reliability of the testimony to be provided by Cheek's experts. *Daubert* set forth four non-exclusive factors for consideration in determining whether the reasoning behind expert testimony is reliable: (1) whether the theory presented has been or can be tested; (2) "whether the theory...has been subjected to peer review and publication"; (3) "the known or potential rate of error"; and (4) the amount of

acceptance given to the expert's reasoning or methodology within the relevant professional community. *Daubert*, 509 U.S. at 593-594.

The Third Circuit in *Paoli* further articulated that the "reliability requirement must not be used as a tool by which the court excludes all questionably reliable evidence." *Paoli*, 35 F.3d at 744 (quoting *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829, 857 (3d Cir. 1990)). The reliability requirement is not centered on whether an expert's conclusions are correct or rest on the "best foundation, but rather whether any particular opinion is based on valid reasoning and reliable methodology." *Kannankeril v. Terminix Int'l.*, 128 F.3d 802, 806-07 (3d Cir. 1997). "'The ultimate touchstone is helpfulness to the trier of fact, and with regard to reliability, helpfulness turns on whether the expert's technique or principle [is] sufficiently reliable so that it will aid the jury in reaching accurate results.'" *Paoli*, 35 F.3d at 744 (citing *DeLuca*, 911 F.2d at 956 (quoting J. Weinstein & M. Berger, *Weinstein's Evidence* 702[03], 702-35 (1988)).

B. ARGUMENT

Wyeth has launched this meritless attack on Cheek's experts in an attempt to have this Court draw an arbitrary line as to where the causal link ends between the use of Wyeth's diet drugs and pulmonary arterial hypertension. Wyeth's argument centers on the fact that no epidemiological study has been conducted to conclusively determine how long the causal link between the diet drugs and pulmonary hypertension lasts. Wyeth unsuccessfully asserted this argument in *Smith* and, having failed in one District Court, now wastes this Court's time in attempting to re-litigate the same fallacious argument in this case. This Court must reject Wyeth's argument because Cheek's experts' causation testimony is rooted in scientifically sound and reliable sources and methods.

Wyeth attacks the reliability of Cheek's experts' causation testimony by attempting to undermine and discredit individual sources and methods that Drs. Rich and Rubin relied on, rather than considering the methodology as a whole. Such an approach is improper. The Federal Judicial Center's *Reference Manual on Scientific Evidence* cautions against this approach and recommends that the court "consider all the relevant available scientific evidence, taken as a whole, to determine which conclusion or hypothesis regarding a causal claim is best supported by the body of evidence." *See* Federal Judicial Center, Reference Manual on Scientific Evidence (3d ed. 2011), The Admissibility of Expert Testimony, p. 20. When the totality of evidence is taken into consideration, the reliability of Cheek's experts' testimony is clear, as they have considered all relevant evidence, and their conclusions are not simply personal opinion but are supported by the evidence.

Cheek's experts' testimony is admissible as it satisfies the requirements for reliability as set forth by the Supreme Court in *Daubert* and the Third Circuit in *Paoli*. As mentioned above, the reliability of Cheek's experts has been previously vetted by a District Court using the *Daubert* standard under an almost identical set of facts, and since the time of the previous decision, developments in the underlying evidence relied on by Cheek's experts only further support admissibility. Indeed, since the publication of IPPHS several large case studies have been published that report on the characteristics of patients with PAH who were exposed to fenfluramines. Each of these studies noted significant latency periods between cessation of diet drug use and the onset of PAH. In many instances the latency periods extended for over ten years. For example, one such study noted that of the reviewed cases, 20% had a latency period of greater than one

year.[18] The authors of another published article reported that the delay between last diet drug intake and the first symptoms of pulmonary hypertension was within two years of exposure in 24% of cases, two to five years in 32% of cases and greater than five years in 43% of cases.[19] Finally, a third study reported a median time between exposure and onset of symptoms of four and one-half years and further noted that a latency period of ten years was quite common.[20] As these three studies demonstrate, the body of medical literature produced since the IPPHS and, importantly, since the *Smith* decision, strongly supports the admissibility of Cheek's experts' opinions.

Furthermore, a hearing is not needed in order to determine reliability, and it is within this Court's purview to decide this case without one. At best, the concerns raised by Wyeth can be addressed by "[v]igorous cross-examination, presentation of contrary evidence, and careful [jury] instruction on the burden of proof." *Daubert*, 509 U.S. at 596. If a line is to be drawn as to where causation ends, it must be drawn by a jury, not by the granting of Wyeth's motion.

1. Cheek's Experts' Causation Testimony Consists of a Testable Hypothesis

Wyeth argues that there is no scientific evidence satisfying the *Daubert* standard that shows that diet drugs can cause PAH nine or more years after cessation or to show that diet drugs caused Cheek's disease. In other words, Wyeth's argument suggests that Cheek's Experts' causation theory can be tested but has not been.

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[18] M. Delcroix et al., *High Incidence of Primary Pulmonary Hypertension Associated with Appetite Suppressants in Belgium*, EUR. RESPIR. J. 12:271, 273 (1998) (Exhibit "O" hereto) (Table 1).
[19] M. Humbert et al., *Pulmonary Arterial Hypertension in France. Results from a National Registry*, 173 AM. J. RESPIR. CRIT. CARE MED. 9:1023, 1025 (2006) (Exhibit "P" hereto).
[20] Souza, *supra* note 11.

While no study has been performed to determine the exact length of the causal link between ingestion of fenfluramines and PAH, IPPHS was a controlled study designed to test if a causal link existed between the drugs and pulmonary hypertension. Higenbottam Dep. 74:5-76:16, June 25, 2012 (Exhibit "Q" hereto); Rich Dep. 146:1-147:14, June 11, 2012 (Exhibit "R" hereto). Wyeth does not dispute that IPPHS established an association and causal link between ingestion of fenfluramines and developing PAH. However, they do question the reliability of Cheek experts' reliance on IPPHS to conclude that diet drugs caused Cheek's PAH because her disease was diagnosed over ten years after last ingestion of the drugs. This is not a basis for exclusion of the testimony as unreliable, but a subject for cross-examination.

The Third Circuit has held "that the district court [can]not exclude the testimony simply because the conclusion [is] 'novel' if the methodology and the application of the methodology [are] reliable.... [A] district court must examine the expert's conclusions in order to determine whether they could reliably follow from the facts known to the expert and the methodology used." *Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 153 (3d Cir. 1999) (citing *Paoli*, 35 F.3d at 746 n.15).

It is well recognized that:

> For disease processes with long latency periods, valid studies cannot be performed until the disease has manifested itself. As a consequence, some plaintiffs may be forced to litigate long before epidemiologic research is available. Indeed, sometimes epidemiologic evidence is impossible to obtain, which may explain why neither the plaintiff nor the defendant is able to proffer supportive epidemiology. Thus, most courts have appropriately declined to impose a threshold requirement that a plaintiff always must prove causation with epidemiologic evidence.

Restatement (Third) of Torts: Liab. for Physical and Emotional Harm § 28 cmt. c (2010).

The non-existence of an epidemiological study directly addressing latency here should *not* be viewed as dispositive of causation, and as explained above in the Restatement (Third) of Torts, a disease process with a long latency period cannot be validly studied until the disease manifests itself. *See id.* While Wyeth complains about the ongoing litigation involving its diet drugs fourteen years after removal from the market, this litigation is merely a side-effect of the fact that the disease caused by Wyeth's product may not become apparent for many years following exposure to the drug. *See* Def.'s Mot, 1-2. Without the findings of IPPHS, whose relevance to the causation question generally Wyeth does not challenge, the scientific and medical community would not have any reliable basis for concluding that a causal link between the diet drugs and PAH exists.

Furthermore, differential diagnosis, which was the methodology used by Cheek's experts to conclude that Wyeth's diet drugs caused her PAH, is also based on a testable hypothesis and satisfies the first guidepost of *Daubert*. The Third Circuit in *Paoli* explained that "differential diagnosis can be considered to involve the testing of a falsifiable hypothesis… through an attempt to rule out alternative causes." *Paoli*, 35 F.3d at 758.

2. Cheek's Experts' Theory has Been Subjected to Peer Review and Publication

Wyeth's argument consistently goes back to its belief that no reliable evidence exists that supports Cheek's experts' testimony that diet drugs can cause PAH nine or more years after a patient's exposure. Contrary to Wyeth's argument, Cheek's experts' testimony is not only derived from peer-reviewed and published works, but Cheek's experts have also published peer-reviewed works and studies on the relationship between

diet drugs and pulmonary hypertension. While not conclusive of reliability, "submission to the scrutiny of the scientific community is a component of 'good science'...." *Daubert*, 509 U.S. at 593.

IPPHS, which conclusively established a causal link between Wyeth's drugs and pulmonary hypertension, was extensively peer-reviewed and published in the New England Journal of Medicine.[21] The case studies, case registries, and case reports that Cheek's experts relied on and considered in conjunction with other evidence were also published after being subject to peer review.[22] Additionally, Dr. Rich and Dr. Rubin have each published articles on pulmonary hypertension in the peer-reviewed literature. These articles detail the nature of the causal relationship between the disease and the diet drugs.[23] Dr. Rich also wrote the chapter on pulmonary hypertension in a leading medical textbook.[24] In that chapter, he stated that "pulmonary hypertension will develop years after the last exposure [to the diet drugs]." *Id.* These published works all went through extensive peer review before publication, and thus, support the reliability of Cheek's experts' testimony. When discussing the peer review and publication aspect of Dr. Rich's reliability, the court in *Smith* stated that "Defendant does not seriously question that Plaintiff's expert, Dr. Rich, either authored, or otherwise contributed to, most of the publications in the discipline." *Smith,* 278 F. Supp. 2d at 696.

While Cheek's experts' differential diagnoses of her PAH has not been subject to peer review, the court in *Paoli* recognized that the medical community rarely considers the reliability of the differential diagnosis of an individual; rather, reliability is

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[21] Abenhaim, *supra* note 16.
[22] Souza, *supra* note 11; Humbert, *supra* note 19; Rich, *supra* note 17.
[23] *See* Exhibits J & K.
[24] *Harrison's Principles of Internal Medicine*, Chapt. 250, 2076-82 (D. L. Longo et al., eds., 18th ed. 2012).

determined by a doctor's utilization of standard diagnostic techniques. *Paoli*, 35 F.3d at 758. Dr. Rubin's and Dr. Rich's differential diagnoses are consistent with standard diagnostic practice as evidenced by the Dana Point Classification System, which was subjected to peer review. A diagnosis of IPAH, when a patient has been exposed to Wyeth's diet drugs, is irreconcilable with the consensus of the medical community as established in the Dana Point classification, which requires attribution to any "definite" risk factors, including diet drugs. *See supra* pp. 5-6. The reliability of Cheek's experts' testimony is only further strengthened by the second guidepost of *Daubert*.

3. The Known or Potential Rate of Error Does Not Make Experts' Testimony Unreliable

Since Cheeks experts' testimony relies on numerous studies and publications, there is no easily identifiable rate of error that can be applied to their reasoning. However, Wyeth contends that Cheek's experts have erred in coming to their conclusions, specifically as those conclusions rely on IPPHS. Wyeth erroneously asserts that no risk existed after one year and further asserts that Cheek's experts' reliance on IPPHS is improper because the IPPHS overall 6.3 risk-odds ratio should not be applied to persons in Cheek's position. Rather, Wyeth points to the "past users" subgroup, which had a risk-odds ratio of 2.4, albeit it with broad confidence intervals due to the small number (seven) of patients in that subgroup. Additionally, Wyeth points to Dr. Rich's previous testimony as being inconsistent in terms of how long the latency period may be as further evidence of a lack of reliability. Wyeth also challenges Cheek's experts' differential diagnosis as being unreliable and errant for not accounting for idiopathic causes. However, these arguments are based on Wyeth's misconstruction and misinterpretation of Cheek's experts' testimony.

i. Cheek's Experts' Reliance on IPPHS is Proper

While IPPHS did not explicitly address the question of latency presented here, IPPHS did establish that diet drugs cause PAH and provided evidence that this link continues to exist a year or more after the last exposure to the diet drugs. Cheek's experts agree that the risk dissipates over time, but a decline in risk does not mean that the risk falls back to the background population rate for pulmonary hypertension. Despite Wyeth's best efforts at blurring this distinction, a decline in risk cannot be equated with an exclusion of causation. Within a 95% confidence interval, IPPHS conclusively determined that the risk-odds ratio of developing pulmonary hypertension after taking the diet drugs was 6.3.[25] Subset analysis was later performed in an attempt to determine if any statistically significant odds ratios could be ascertained for individual factors, including past users (those who had discontinued use of diet drugs for more than one year) and long-term users (those who ingested diet drugs for more than one year). This analysis determined a 2.4 risk-odds ratio for past users and a 42 risk-odds ratio for long-term users.

While the 2.4 risk-odds ratio is not statistically significant, it still provides evidence that the causal link between diet drug use and developing pulmonary hypertension continues to exist one year or more after last ingestion of the drugs. There is a significant distinction between finding no risk and failing to obtain a statistically significant result for a small subset. Indeed, Wyeth's expert conceded that IPPHS showed that, statistically, use of fenfluramines would more likely double or triple the risk of developing pulmonary hypertension than the likelihood of the drugs having no effect

[25] *See* Rich Dep. 183:6-11, June 11, 2012.

at all. Higenbottam Dep. 129:10-15, June 25, 2012.[26] Additionally, the IPPHS risk-odds ratio of 42, for users who took fenfluramines for over a year, provides evidence that the longer the diet drugs are taken the higher the risk will be. Conveniently, Wyeth fails to mention that Cheek also fits into this subgroup with a whopping 4200% increased chance of developing pulmonary hypertension. Because Cheek fits into both of these categories, therefore, there is reliable evidence that her risk would be greater than the overall risk for all users because she took the medicine for over a year – even if that risk declined over time.

Data does not necessarily have to be statistically significant in order to be used to bolster an expert's inference of causation, as long as it is not the sole source of support. *In re Avandia Mktg., Sales Practices & Prods. Liab. Litig.*, MDL No. 1871, 2011 U.S. Dist. LEXIS 479 *13 (E.D. Pa. Jan. 4, 2011). Similarly, the United States Supreme Court recently clarified that "[a] lack of statistically significant data does not mean that medical experts have no reliable basis for inferring a causal link between a drug and adverse events . . . . '[M]edical professionals and researchers do not limit the data they consider to the results of randomized clinical trials or to statistically significant evidence.'" *Matrixx Initiatives, Inc. v. Siracusano*, 131 S. Ct. 1309, 1319 (2011) (quoting Brief for Medical Researchers as *Amici Curiae* 31). IPPHS was not powered to determine long-term latency, but it was designed to establish causation. Rich Dep. 179:21-24, June 11, 2012; Higenbottam Dep. 74:5-15, June 25, 2012. It defies basic logic to suggest that the risk exists on Day 364 and not on Day 366. *See Smith,* 278 F. Supp. 2d at 694-95.

[26] Dr. Higenbottam agrees that "statistical nonsignificance is often misunderstood as meaning that the study was negative or that it failed to detect an effect." *Id.* at 129:20-130:5.

Cheek's experts have properly considered all the potentially applicable subgroups in opining that the risk of PAH continues to exist after one year.

Furthermore, Wyeth's assumption that the past users subgroup is the most appropriate subset applicable to Cheek is bad science. Wyeth conveniently focuses on this subset, which has a risk-odds ratio of 2.4, and fails to mention that Cheek would also be included in the subset of individuals who took diet drugs for one year or more, which had a risk-odds ratio of 42. *See* Rich. Dep. 176:6-14, June 11, 2012 (explaining that it is an improper use of IPPHS to focus on single subgroups because individual patients fall into more than one subset). Because an individual will fall into more than one subset, Cheek's experts have testified and explained that the 6.3 risk-odds ratio is the most applicable to Ms. Cheek because it takes into account both the duration of her diet drug use and the latent period before her PAH diagnosis. *Id.*

Cheek's experts do not contend that the 6.3 risk-odds ratio found in IPPHS is necessarily the only risk-odds ratio applicable to Cheek. Rather, the 6.3 risk-odds ratio is the most accurate risk-odds ratio to apply to diet drug users *in general* because this ratio accounts for all of the factors measured in the study. *See* Rich Dep. 41:13-42:9, June 11, 2012; Rubin Dep. 16:13-17:12, June 20, 2012. Cheek's experts, however, do not rely solely on the 6.3 risk-odds ratio for their causation opinions in this case because IPPHS was not designed or powered to determine how long the risk of developing diet-drug-induced PAH continues.

ii. Cheek's Experts' Prior Testimony on Latency Does Not Support the Proposition that their Testimony in this Matter is Unreliable

Wyeth's absurd argument that Dr. Rich's previous testimony shows a lack of reliable evidence relies solely on taking Dr. Rich's statements out of context and misconstruing them to support their fallacious argument. Even more ludicrous is Wyeth's incorrect assertion that there is no new underlying evidence that could account for any change in Cheek's experts' opinions. Despite Wyeth's protestations, Dr. Rich has never testified to an absolute outer limitation to the latency period between the last diet drug usage and the development of PAH, and Wyeth is unable to point to any of Dr. Rich's past testimony to credibly support its contention. Wyeth pointed to Dr. Rich's testimony in *Burt* as support for its argument, but Dr. Rich has clarified that his statements only meant that, at the time of *Burt*, he was sure that the latency window was *at least* five years. Rich Dep. 118:1-10, June 11, 2012; Rich Dep. 63:21-64:4, June 4, 2002 (Wyeth's Exhibit OO). Furthermore, Dr. Rich clearly testified that since the time of his testimony in that case in 2002 there has been additional information including the "French Registry Report, … French Experience Report, … SOPHIA experience, and [his] own personal experience." Rich Dep. 68:20-69:3, June 11, 2012 (citing studies that have been published since 2002 where he has consistently seen patients with diet drug exposures ten years out having PAH related to the diet pills). This additional evidence clearly accounts for any development in Dr. Rich's expert opinion on the latency window for PAH to develop after diet drug use.

iii. Cheek's Experts' Differential Diagnosis is Not Unreliable Because of their Claimed Failure to Conclusively Rule Out Idiopathic Causes

Dr. Rich's and Rubin's independent differential diagnoses of Cheek with diet-drug-induced pulmonary hypertension are based on the evidence provided by IPPHS, medical and scientific literature, their extensive clinical experience, and on the elimination of alternate causes of pulmonary hypertension, including unknown causes. Wyeth's argument that Cheek's experts offered no explanation for ruling out IPAH as a cause of Cheek's PAH is flawed from the outset. By Wyeth's own admission, IPAH is a *diagnosis* – not a cause – given to pulmonary hypertension when the cause is unknown. *See* Wyeth's Motion, at p. 2; *see generally* Simonneau, *supra* note 12. Therefore, Wyeth's argument on its face challenges the conclusions of Cheek experts' diagnoses rather than their methodology – a faulty approach under *Daubert*.

In *Paoli,* in holding that differential diagnosis was a reliable method, the court stated that differential diagnosis "does not frequently lead to incorrect results." *Paoli*, 35 F.3d at 758. Furthermore, the court held that the use of differential diagnosis to come to a novel conclusion does not make it unreliable. *Id.* at 759 n.27; *see also Heller*, 167 F.3d at 156 (citing *Paoli*). The court did note that if a defendant points to a plausible alternative cause, the expert must provide an explanation as to why he concluded that was not the cause. *Paoli*, 35 F.3d at 760-62. While expounding on the reliability of differential diagnosis in *Heller*, the Third Circuit explained that only minimal explanation is needed to overcome a defendant's assertion of an alternate cause. *See Heller*, 167 F.3d at 156-57. As the court explained, Plaintiff's experts need not offer detailed explanations for their diagnoses but merely need to offer more than "no explanation." *Id.* at 156

(quoting *Paoli*, 35 F.3d at 759 n.27). In making a proper differential diagnosis, a doctor does not have to rule out every alternative possible cause, as long as they use "sufficient diagnostic techniques to have good grounds for his or her conclusion." *Id.* at 156 (quoting *Paoli*, 35 F.3d at 761). Furthermore, a study that has explicitly determined how long the latent period may be after drug cessation is not necessary for a differential diagnosis as courts have held that:

> experience with hundreds of patients, discussions with peers, attendance at conferences and seminars, detailed review of a patient's family, personal, and medical histories, and thorough physical examinations are the tools of the trade, and should suffice for the making of a differential diagnosis even in those cases in which peer reviewed studies do not exist to confirm the diagnosis of the physician.

Johnson v. Vane Line Bunkering, Inc., No. 01-5819, 2003 U.S. Dist. LEXIS 23698, at *24 (E.D. Pa. Dec. 30, 2003) (quoting *Heller*, 167 F.3d at 155).

Cheek acknowledges that a differential diagnosis is not an exact science and that any such diagnosis includes some potential for error, but Cheek's experts have offered more than sufficient explanations for their conclusions that her PAH *more likely than not* resulted from diet drugs rather than an unknown cause. In making his diagnosis that Cheek's pulmonary hypertension was caused by diet drug use rather than idiopathic causes, Dr. Rich testified that he primarily looked to the temporal relationship between the drugs and the amount of the exposure. *See* Rich Dep. 37:6-40:8, June 11, 2012 (Describing the risk after prolonged exposure as being very high, possibly the highest risk in all of medicine, and that if someone took diet drugs more than 12 months, developing PPH is "almost a certainty"). His differential diagnosis takes into account not only Cheek's medical records but also IPPHS, case reports, other scientific literature, and his own personal clinical observations. Based on all of this evidence, Dr. Rich was able to

opine with a high degree of medical and scientific certainty that Cheek's PAH was caused by diet drugs. *Id.* at 173:4-6.

Dr. Rubin also explained the basis for his differential diagnosis. While recognizing that IPAH can never be completely excluded, Dr. Rubin bases his diagnosis on the strong evidence that demonstrates that when an individual takes diet drugs and develops PAH, then the diet drugs are more likely than not the cause. *See* Rubin Dep. 14:17-17:12, June 20, 2012. The evidence considered by Dr. Rubin includes epidemiological data, clinical data, and basic scientific data. *Id.* at 14:17-15:7, 25:18-26:8. This allowed him to conclude that the diet drugs more likely than not caused Cheek's PAH. *Id.* The information relied on was not solely IPPHS or case reports, but it was the "totality of the medical and scientific literature" that allowed him to conclude that Cheek's PAH was caused by diet drugs. *See id.* at 25:18-26:8. Furthermore, Dr. Rubin testified that it is not biologically plausible that the risk of diet drugs causing PAH goes to zero at one year. *Id.* at 24:7-20. This testimony clearly provides an explanation as to why Dr. Rubin concluded that diet drugs caused Cheek's PAH and why it did not result from unknown or idiopathic causes.

Cheek's experts have adequately explained the basis of their diagnoses of PAH caused by diet drugs to surmount the *Daubert* hurdle. Because Cheek's experts have considered all relevant evidence, which suggests that diet drugs are more likely the cause of Cheek's PAH, their differential diagnoses satisfy the admissibility requirements of *Daubert* and *Paoli*, and the possibility of error should not deem them so unreliable as to become inadmissible. Wyeth's suggestion of IPAH causes goes to the weight of the expert testimony proffered and not its admissibility, since IPAH has been adequately

addressed by Cheek's experts. Indeed, even had Cheek's experts not considered IPAH, Wyeth's argument would still be without merit. The United States District Court for the Eastern District of Pennsylvania has held that an expert's failure to consider an idiopathic origin of a disease should not result in the exclusion of the expert's opinion and that the suggested alternative cause should only affect the weight that the jury gives the expert testimony. *Larson v. Bondex International (In re Asbestos Prods. Liab. Litig.)*, MDL No. 875, 2010 U.S. Dist. LEXIS 123090, at *13-14, (E.D. Pa. Nov. 15, 2010) (citing *Heller*).

4. Cheek's Experts' Causation Theory is Generally Accepted in the Relevant Scientific and Medical Communities

The lynchpin of Wyeth's argument focuses on the fourth guidepost of *Daubert*, general acceptance. Wyeth states there is "no reliable, generally accepted evidence or methodology showing that diet drugs can cause PPH nine or more years after a patient stops taking them." Def.'s Mot. 17. Wyeth's argument revolves around the credibility of Dr. Rich's and Dr. Rubin's conclusions based on Wyeth's critique of the individual sources they relied on in arriving at their opinions, rather than considering the evidence in its entirety. Exclusion of Cheek's Experts' testimony is not the proper way for Wyeth to combat these concerns; rather, they must present these issues to the jury for resolution.

The Supreme Court's decision in *Daubert* overruled the requirement that an expert opinion must be generally accepted in order to be admissible and held that expert testimony must be supported by appropriate validation or "good grounds." *Daubert*, 509 U.S. at 590 (quoting Webster's Third New International Dictionary 1252 (1986)). However, Dr. Rich's and Dr. Rubin's causation opinions and differential diagnosis *are* generally accepted in the relevant scientific and medical communities, and Wyeth has not pointed to a scintilla of evidence to the contrary, other than its own litigation experts.

i. IPPHS is Generally Accepted as Having Established a Causal Link Between Diet Drugs and Pulmonary Hypertension; The Disagreement on the Interpretation of this Study Goes to the Weight of the Evidence Not Its Admissibility

As Dr. Rich testified, studies and peer-reviewed papers after IPPHS have not addressed the issue of causation because it was proven by IPPHS. *See* Rich Dep. at 85:3-86:15 June 11, 2012. IPPHS is generally accepted as having established a causal link between Wyeth's drugs and pulmonary hypertension. Defendant's expert described IPPHS as "the most salient epidemiological data with respect to an association between diet drugs and PPH." Levine Expert Report ¶ 14 (Exhibit "S" hereto). Further support of IPPHS' general acceptance is evident from its publication and in the well-respected New England Journal of Medicine.[27] While IPPHS did not directly address latency, its general acceptance for discovering the causal link between diet drugs and pulmonary hypertension is integral to any causation opinion. IPPHS, when considered with the totality of evidence including other medical literature and the experts' clinical experience, is sufficiently reliable evidence of causation to render the opinions of Drs. Rich and Rubin admissible under *Daubert.*

Further support of IPPHS' general acceptance, reliability, and importance to Cheek's case is that IPPHS was the seminal study relied on, not only by Cheek's experts, but by Wyeth's experts as well. *See* Higenbottam Expert Report, at pp. 4-5 (Exhibit "T" hereto); Levine Expert Report, ¶¶ 14-17. Dr. Levine's expert opinion is almost entirely derived from his interpretation of the data and statistics of IPPHS.[28] Dr. Levine uses the risk-odds ratios of the IPPHS post-hoc subgroups in order to come to the conclusion that

[27] Abenhaim, *supra* note 12.
[28] *See* Levine Expert Report ¶ 14; *see generally id.* at ¶¶ 15-23 (explaining use of risk-odds ratios and his interpretations).

the risk of PAH declines over time. *See* Levine Expert Report, ¶¶ 20-23. Dr. Higenbottam also relies heavily on the IPPHS study in which he participated and interprets it as confining the risk to only one year after cessation. *See* Higenbottam Expert Report, at p. 14. The significant function that IPPHS serves to both Cheek's and Wyeth's experts speaks highly of its reliability. By attempting to discredit the reliability of Cheek's experts' testimony based on their consideration of IPPHS, Wyeth is essentially undermining the reliability of its own experts' testimony. Differing conclusions and interpretations by experts are not proper grounds for exclusion of their testimony; rather, they are issues of credibility, which is not a factor of admissibility. *See In re TMI Litig.*, 193 F.3d 613, 713 (3d Cir. 1999) (holding that the district court had "conflated its gatekeeping function with the fact-finder's function as the assessor of credibility" by excluding plaintiff's expert's testimony for using what the district court considered a less credible latency period in his analysis).

The conflict between Cheek's and Wyeth's experts' testimonies should not be construed as a lack of general acceptance of Cheek's experts' causation opinion, but rather as a conflict for the jury to consider when weighing the experts' testimonies. Conflicting opinions and conclusions of opposing expert witnesses are not uncommon. Resolution of a "battle of the experts" is "a factual interpretation [that] is within the province of a jury." *Rooney v. City of Philadelphia*, 623 F. Supp. 2d 644, 656 (E.D. Pa. 2009). The jury is the body tasked with deciding how much weight should be attributed to an expert's testimony. 32A C.J.S. Evidence § 1006 ("Where conflicting expert testimony is presented, it is the obligation of the jury to determine the credibility of the witnesses and to weigh their testimony"). The heart of Wyeth's argument revolves

around the credibility and conclusions of Dr. Rich's and Dr. Rubin's testimony based on Wyeth's dissection and interpretation of the individual sources Cheek's experts relied on in arriving at their opinions. Exclusion of their testimony is not the proper way for Wyeth to combat these concerns; rather, they must present these issues to the jury for resolution.

ii. Cheek's Experts' Consideration of Case Reports is Generally Accepted

Dr. Rich's and Dr. Rubin's consideration of published and peer-reviewed case studies, case registries, and case reports is consistent with generally accepted practices. *See* Rich Dep. 85:8-23, June 11, 2012; Rubin Dep. 33:8-9, June 20, 2012. Specifically, Cheek's experts reference case reports such as that of Dr. Souza, studies such as SOPHIA and SNAPH, along with a multitude of publications by other pulmonary hypertension experts on the issue of diet-drug-induced PAH, to support their assertion that, despite the more than ten years between Cheek's last ingestion of diet drugs and her diagnosis of PAH, the latter is attributed to the former.[29] While such reports *alone* are not intended to and cannot determine the existence of a causal relationship, they are an invaluable resource that provides information on the effects of diet drug use in real-world clinical settings. Furthermore, the case reports were not used to establish a causal relationship between diet drugs and pulmonary hypertension as that was accomplished by IPPHS. Rather, these reports and studies give further insight on the nature of the causal link. Furthermore, Cheek's experts considered these studies and reports in conjunction with the other evidence discussed herein, and their reliability cannot be determined in isolation from the other evidence relied on by Drs. Rich and Rubin. *See* Rubin Dep. 33:8-9, June

[29] Souza, *supra* note 11; Walker, *supra* note 14; Rich, *supra* note 17.

20, 2012 ("IPPHS coupled with these case reports, basic science, subsequent clinical observations, taken together are strong evidence of a link.").

Courts have recognized the generally accepted use of case reports when "carefully considered in light of other information available." *Wolfe v. McNeil-PPC, Inc.*, No. 07-348, 2011 U.S. Dist. LEXIS 47710, at *15 (E.D. Pa. May 4, 2011) (quoting *Reference Manual on Scientific Evidence* 475 (2d ed. 2000)). As recognized in *Wolfe*, case reports "contribute to the reliability of a causation determination." *Id.* (quoting *Deutsch v. Novartis Pharm. Corp.*, 768 F. Supp. 2d 420, 476 (E.D.N.Y. 2011)). Non-epidemiological sources are often used by experts in rendering scientific opinions, and the evidence "should be considered by the court in assessing the reliability of those opinions." *In re Phenylpropanolamine (PPA) Prods. Liab. Litig.*, 289 F. Supp. 2d 1230, 1242 (W.D. Wash. 2003); *see also Rider v. Sandoz Pharms. Corp.*, 295 F.3d 1194, 1202 (11th Cir. 2002) (agreeing with the district court that a large number of case reports may be reliable evidence). Furthermore, the fact that these case reports, case registries, and case studies appeared in peer-reviewed publications further evidences their general acceptance in the relevant medical and scientific communities. The case reports are simply another brick in the wall of evidence that Cheek's experts considered in arriving at their causation opinions, and the reports' limited part in the development of Cheek's experts' testimony does not make it unreliable.

iii. Cheek's Experts' Differential Diagnosis

There is no dispute between the parties that differential diagnosis is a generally accepted methodology under Third Circuit precedent. While Cheek's individual diagnosis has not been put forth as a candidate for general acceptance, an individual

diagnosis is rarely generally accepted. Rather, the reliability of an individual diagnosis is determined by looking at the general acceptance of the diagnostic measures taken by the experts. *See Paoli*, 35 F.3d at 758-759. As previously discussed in Section II (B), the attribution of Cheek's pulmonary hypertension to diet drugs is consistent with the Dana Point Classification System, which was developed at a World Symposium on pulmonary hypertension. This symposium was attended by the leaders in the field, and their development of this classification is strong evidence of the general acceptance of the standards applied by Cheek's Experts.

Furthermore, Cheek's experts have reviewed her medical records and have ruled out all other known causes of pulmonary hypertension. The possibility of an idiopathic cause has been accounted for by the experts, and it is unnecessary for Cheek's experts to conclusively rule out an idiopathic cause since an explanation has been provided. *See Heller,* 167 F.3d at 155-57. As with all of Wyeth's arguments, suggestion of IPAH goes to the weight of the expert testimony proffered and not its admissibility.[30]

5. Additional Factors Recognized by the Third Circuit Further Support the Reliability of Cheek's Experts' Testimony

In addition to satisfying the four guideposts of *Daubert*, the satisfaction of several of the factors established by the Third Circuit further support the reliability of Cheek's Experts' testimony.[31] Wyeth criticizes the methodology utilized by Cheek's experts, but Wyeth does not present any methodology or technique that would be more reliable in

[30] In *Larson v. Bondex Int'l (In re Asbestos Prods. Liab. Litig.)*, 2010 U.S. Dist. LEXIS 123090, *13-14, (E.D. Pa. Nov. 15, 2010), the court held that an expert's failure to consider an idiopathic origin of a disease should not result in the exclusion of the expert's opinion and that the suggested alternative cause should only affect the weight that the jury gives the expert testimony.

[31] Of the additional factors mentioned here, the most applicable are the qualifications of the expert and relation of methodology to other more reliable techniques. *See supra* p. 15. However, the existence and maintenance of standards could be applied to experts' differential diagnoses in connection with Dana Point, but this has already been exhaustively covered above.

ascertaining the cause or latent nature of Cheek's pulmonary hypertension. Furthermore, Wyeth does not address the qualifications of Cheek's experts – qualifications which also speak to the reliability of their testimony.

Even though Wyeth has questioned the reliability of Cheek's experts' methods, Wyeth has failed to point to any methodology or technique that is more reliable. While the burden of proof to prove reliability is the responsibility of the Plaintiff, Wyeth fails to mention an alternative methodology because none exists. While both parties' experts have acknowledged that there is no diagnostic test to distinguish IPAH from diet-drug-induced PAH, Cheek's experts have considered all relevant and reliable evidence in arriving at their opinion, and thus, their opinion is based on almost the same information as Wyeth's experts. When viewed in this light, it is easier to see what Wyeth truly challenges is not the evidence or methodology used by Cheek's Experts, but rather challenges Cheek's experts' conclusions. Such challenges are improper.

The focus of the reliability requirement is on the *methodology* used by an expert not on the "merits of the conclusion drawn." *Main St. Mortg., Inc. v. Main St. Bancorp., Inc.*, 158 F. Supp. 2d 510, 514 (E.D. Pa. 2001). Third Circuit case law supports the idea that:

> The judge should not exclude evidence simply because he or she thinks that there is a flaw in the expert's investigative process which renders the expert's conclusions incorrect. The judge should only exclude the evidence if the flaw is large enough that the expert lacks "good grounds" for his or her conclusions.

In re Orthopedic Bone Screw Prods. Liab. Litig., MDL No. 1014, 1997 U.S. Dist. LEXIS 6441, *13 (E.D. Pa. May 5, 1997) (quoting *Paoli*, 35 F.3d at 746). Cheek's experts'

methodology is based on established scientific and medical principles; this is not the type of "junk science" that *Daubert* is meant to exclude.

Additionally, Cheek's experts' qualifications and clinical experience further support the reliability of their testimony on the causation of Cheek's pulmonary hypertension. *See* Rich Dep. 71:23-72:6, June 11, 2012; Rubin Dep. 33:3-9, June 20, 2012. Dr. Rich and Dr. Rubin are two of the foremost experts in the world on pulmonary hypertension and have devoted their careers to improving the treatments and the procedures for diagnosing the disease. Their testimony and opinions are not speculation but are supported by their own and others' research, peer-reviewed papers, and clinical observations.[32]

The Third Circuit has held that an expert doctor's experience can render the expert's testimony reliable and, therefore, admissible as evidence.[33] The expertise of Drs. Rich and Rubin is strong evidence of reliability and should be an important factor in the court's decision. [34] While the experts' qualifications are not the only basis for the admissibility of their testimony under *Daubert*, their experience is unparalleled and far exceeds the "good grounds" basis needed to satisfy the *Daubert* standard.

* * *

[32] Rich Dep. 132:4-9, June 11, 2012 ("I'm saying this is my opinion as an expert who has been involved in this disease for 34 years, who didn't read the IPPHS and didn't read SNAP and didn't read SOPHIA. I lived it.... I designed it. I went through all the data. I reviewed it."); Rubin Dep. 33:8-9, June 20, 2012 ("IPPHS coupled with these case reports, basic science, subsequent clinical observations, taken together are strong evidence of a link.").

[33] *Schneider v. Fried*, 320 F.3d 396, 406 (3d Cir. 2003) (In pointing out that a doctor's experience may be good reason to admit his testimony, the Court stated "[w]here there are other factors that demonstrate the reliability of the expert's methodology, an expert opinion should not be excluded simply because there is no literature on point.").

[34] *See Keller v. Feasterville Family Health Care Ctr.*, 557 F. Supp. 2d 671, 677 (E.D. Pa. 2008) (holding that an expert's qualifications are helpful "in establishing the reliability of his methodology"); *Lillis v. Lehigh Valley Hosp., Inc.*, No. 97-3459, 1999 U.S. Dist. LEXIS 13933, at *21 (E.D. Pa. Sept. 3, 1999) (holding that an expert's testimony is not unreliable just because it is not substantiated in literature and that an expert's experience and knowledge can demonstrate that his testimony is reliable).

Cheek's experts' testimonies satisfy the flexible *Daubert* standard and its reliability requirement. Dr. Rich's and Rubin's testimonies are derived from their review of all relevant scientific literature and their personal experience. A causal link has been conclusively established between the diet drugs and PAH. Exactly how long this link persists has not been pinpointed. However, based on reliable scientific evidence and methods, Cheek's experts have opined that the causal link extends at least to the time frame in which Ms. Cheek developed pulmonary hypertension after taking diet drugs. While Wyeth posits that this is an "analytical gap" "between the data and the opinion proffered," there are no gaps when the totality of evidence is considered. *See Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997). Indeed, in light of all of the evidence and experience relied upon, the causation testimony proffered by Drs. Rich and Rubin has a strong and reliable foundation and will help the trier of fact understand the nature of the link between ingesting diet drugs and developing pulmonary hypertension.

V. JAMIE CHEEK'S DIAGNOSIS OF PULMONARY ARTERIAL HYPERTENSION PASSES THE THREE-PART TEST REQUIRED BY THE NATIONAL SETTLEMENT AGREEMENT. THEREFORE, ENJOINING HER CASE PURSUANT TO PRETRIAL ORDER NO. 2383 IS IMPROPER.

Wyeth contends that this Court should enjoin Plaintiff Cheek's case on the grounds that her suit is barred pursuant to the NSA for failing to meet the specific diagnostic criteria for PAH contained therein. However, Ms. Cheek's PAH diagnosis satisfies the threshold requirements set forth in the NSA for bringing a claim against Wyeth, and, as a result, enjoining her case would be improper.

A. Three-Part Test Required by NSA

The intent of the NSA was to limit Wyeth's liability exposure for claims arising from diet-drug-related injuries, while also preserving the claims of those who develop diet-drug-related diseases by establishing a method for determining whether their development of PAH or valvular heart disease (the two diseases related to fenfluramine and/or dexfenfluramine exposure) is sufficiently related to their diet drug use to warrant pursuit of a claim for compensation for their injuries. With this goal in mind, Wyeth and Class Counsel agreed on a three-part test that must be met in order to pursue a PPH claim. Part One requires only one of the following:

> Mean pulmonary artery pressure by cardiac catheterization of ≥ 25 medical monitoring Hg at rest or ≥ 30 medical monitoring Hg with exercise with a normal pulmonary artery wedge pressure ≤ 15 medical monitoring Hg; or
>
> A peak systolic pulmonary artery pressure of ≥ 60 medical monitoring Hg at rest measured by Doppler echocardiogram utilizing standard procedures; or
>
> Administration of Flolan to the patient based on a diagnosis of PPH with cardiac catheterization not done due to increased risk in the face of severe right heart dysfunction[35]

In addition to meeting at least one requirement of Part One, Part Two of Section I.46 also requires that a plaintiff must present the following:

> Medical records which demonstrate that the following conditions have been excluded by the following results:
>
> (a) Echocardiogram demonstrating no primary cardiac disease including, but not limited to, shunts, valvular disease (other than tricuspid or pulmonary valvular insufficiency as a result of PPH or trivial, clinically insignificant left-sided valvular

[35] *In re Diet Drugs Prods. Liab. Litig.*, 2000 U.S. Dist. LEXIS 12275, at *87 (E.D. Pa. Aug. 28, 2000) (quoting NSA § I.46).

regurgitation), and congenital heart disease (other than patent foramen ovale); and

(b) Left ventricular dysfunction defined as LVEF < 40% defined by MUGA, Echocardiogram or cardiac catheterization; and

(c) Pulmonary function tests demonstrating the absence of obstructive lung disease (FEV_1/FVC > 50% of predicted) and the absence of greater than mild restrictive lung disease (total lung capacity > 60% of predicted at rest); and

(d) Perfusion lung scan ruling pulmonary embolism; and

(e) If, but only if, the lung scan is indeterminate or high probability, a pulmonary angiogram or a high resolution angio computed tomography scan demonstrating absence of thromboembolic disease[36]

Finally, Part Three of the PPH diagnosis definition set forth in the NSA requires that:

> Conditions known to cause pulmonary hypertension including connective tissue disease known to be causally related to pulmonary hypertension, toxin induced lung disease known to be causally related to pulmonary hypertension, portal hypertension, significant obstructive sleep apnea, interstitial fibrosis (such as silicosis, asbestosis, and granulomatous disease) defined as greater than mild patchy interstitial lung disease, and familial causes, have been ruled out by a Board-Certified Cardiologist or Board-Certified Pulmonologist as the cause of the person's pulmonary hypertension.[37]

B. Jamie Cheek's PAH Diagnosis

The three-part PPH definition provided in the NSA is an exemplary model for the process of differential diagnosis as it relates to PPH – the same process that was utilized for diagnosing Jamie Cheek's PAH. Ms. Cheek was conclusively diagnosed with diet-

[36] *Id.* at *87-88.
[37] *Id.* at *88-89.

drug-induced PAH on May 1, 2008, but this diagnosis followed a battery of tests and diagnostic probing that easily satisfy the three-part PPH definition in the NSA.[38]

First, Ms. Cheek's mean pulmonary artery pressure was 58 mm Hg at her May 1, 2008, right heart catheterization.[39] Likewise, an accurate reading of her pulmonary artery wedge pressure on September 24, 2010, showed it to be 8 mm Hg.[40] These numbers surpass the minimum requirements of Part One of the NSA PPH definition and thus satisfy this initial standard.

Second, Ms. Cheek's medical records clearly demonstrate that the conditions referenced in Part Two of Section I.46 of the NSA have been eliminated as potential causes for Ms. Cheek's PAH. Cheek had multiple echocardiograms, and not one has demonstrated any evidence of a primary cardiac disease (including shunts, valvular disease, and congenital heart disease).[41] Likewise, testing has indicated that Ms. Cheek's left ventricular ejection fraction (LVEF) is consistently greater than 40%, indicating no presence of left ventricular dysfunction.[42] Cheek's pulmonary function tests reveal that she does not have obstructive lung disease.[43] Finally, Dr. Gregory May ruled out the

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[38] MUSC, pp. 13-16 (Plaintiff's cardiac catheterization report from May 1, 2008) (Exhibit "B" hereto); *See also* Plaintiff's First Amended Fact Sheet (hereinafter "PFS"), pp.12-16 (Exhibit "U" hereto) (listing various diagnostic tests performed on Plaintiff from 1998 to 2010).

[39] MUSC, pp. 13-16.

[40] This accurate report followed a previous, inaccurately-interpreted elevated pressure that was originally reported as 16 mm Hg. MUSC, pp. 81-84, 167-168; Highland Dep. 50-52, January 25, 2012 (Exhibit "V" hereto).

[41] PFS, pp.12-16; Plaintiff's Medical Records from Carolinas Hospital (hereinafter "Carolinas"), pp. 5-7 (Exhibit "W" hereto) (Report from March 7, 2008, transesophageal echocardiogram showing no evidence of shunts). Additionally, the March 7, 2008, report makes no mention of valvular disease or congenital heart disease.

[42] Plaintiff's Medical Records from Advanced Cardiology, pp. 17-18 (Exhibit "X" hereto) (Report from October 23, 2009, echocardiogram estimates LVEF between 50 to 55%); MUSC at 44 (reporting LVEF result as 65% based on November 10, 2008, echocardiogram).

[43] *See* MUSC at 44 (reporting FEV_1/FVC as 73% based on a November 10, 2008, pulmonary function test).

possibility that Ms. Cheek suffered from pulmonary embolism ("PE") by performing a CT angiogram on February 19, 2008, which showed no evidence of PE.[44]

Third, two Board-Certified pulmonologists (Dr. Lewis Rubin and Dr. Kristin Highland[45]) and one Board-Certified cardiologist (Dr. Stuart Rich) have ruled out each of the conditions mentioned in Part Three of Section I.46 of the NSA as causes of Ms. Cheek's PAH. Although Ms. Cheek carries a diagnosis of the connective tissue disease known as rheumatoid arthritis ("RA"), it is disputed as to whether this is an accurate diagnosis since Plaintiff is seronegative for rheumatoid factor.[46] Dr. Kristin Highland, also a rheumatologist, points out that Ms. Cheek does not even meet the American College of Rheumatology criteria for RA because she has no positive rheumatoid factor, no positive CCP, and she does not have characteristic x-ray findings or synovitis findings.[47]

However, regardless of whether or not the RA diagnosis is even appropriate, Dr. Kristin Highland, Dr. Lewis Rubin, and Dr. Stuart Rich agree that Ms. Cheek shows no evidence of interstitial lung disease, and, since her RA is not coexistent with interstitial lung disease, it is not the cause of her PAH.[48] Additionally, Ms. Cheek has nothing in her medical history to indicate familial causes of PAH or any form of toxin-induced lung disease, nor did further testing suggest portal hypertension or significant obstructive sleep

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[44] Carolinas, pp. 4-5.
[45] *See* Dr. Kristin Highland's Curriculum Vitae (Exhibit "Y" hereto).
[46] Highland Dep. 73-74, January 25, 2012.
[47] *Id.* at 74; MUSC at 1-5, 33.
[48] Highland Dep. 59-62, 72-75, January 25, 2012; Dr. Lewis Rubin Expert Report (hereinafter "Rubin"), pp. 2-3 (Exhibit "Z" hereto); Dr. Stuart Rich Expert Report (hereinafter "Rich"), p. 3 (Exhibit "AA" hereto).

apnea.[49] As a result, Dr. Highland, Dr. Rubin, and Dr. Rich have likewise excluded those diseases as possible causes of Cheek's PAH.[50]

Therefore, as clearly evidenced above, Plaintiff's PAH diagnosis satisfies the diagnostic threshold established by the NSA and thus permits her to bring this case against Wyeth. In addition to exhibiting the objective measurements set forth in Part One, Cheek's PAH diagnosis mirrors the careful consideration of other known potential causes of PAH, as required by Parts Two and Three.

C. Wyeth's Improper Request to Enjoin Plaintiff's Case

Despite the extensive diagnostic process to which Cheek has been subject, Wyeth argues that Cheek has not sufficiently satisfied the requirements of Part Three of the NSA PPH definition because she has failed to rule out all conditions known to cause PAH. Wyeth's argument relies solely on one phrase contained in the Primary Pulmonary Hypertension Checklist appearing as an appendix to PTO 2383: "[o]ther conditions known to cause pulmonary hypertension."[51] Rather than utilizing the original language provided in the NSA at Section I.46, which reads that proper PAH diagnoses must rule out "conditions known to cause pulmonary hypertension" and which provides a list of such conditions to consider, Wyeth instead distorts the language of a checklist offered by this Court in an appendix to PTO 2383, which was provided as a tool for use in applying the three-part standard of Section I.46 of the NSA.

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[49] *See* MUSC, 1-5 (Dr. Highland's notes from her initial visit with Plaintiff on April 23, 2008, make no mention of a family history of PAH or PH. Additionally, Dr. Highland describes Plaintiff's "environmental exposure history" as "unremarkable[,]" thereby ruling out the possibility that Plaintiff's PAH was toxin-induced. [p. 2.] Although Plaintiff's medical history includes hypertension, there is no mention of a diagnosis of portal hypertension.); *See also* Plaintiff's Medical Records from Carolina Sleep Diagnostics, pp. 1-2 (Exhibit "BB" hereto) (indicating that Plaintiff experiences "*mild* obstructive sleep apnea during REM sleep" [p.2, emphasis added.]).

[50] Highland Dep. 62, 68-70, January 25, 2012; Rubin, pp. 2-3; Rich at 3.

[51] *See* PTO 2383, Appendix B at 3.

Wyeth contends that the phrase "[o]ther conditions known to cause pulmonary hypertension" as it appears in the table attached to PTO 2383 supplements the list of conditions listed in Part Three of NSA Section I.46 to include *all* "other conditions." Wyeth makes this contention despite the fact that the text of PTO 2383 gives no indication of this Court's intent to add to the requirements of Section I.46 of the NSA and, in fact, specifically states that "Appendix B [contains] a chart that sets forth *the requirements of Section I.46a*...."[52] Therefore, the NSA does not require that all other conditions known to cause PAH be ruled out in order to satisfy the three-part definition of PPH that it set forth as a prerequisite for eligibility to pursue a claim against Wyeth. Furthermore, IPAH is not a "condition known to cause pulmonary hypertension." IPAH is not a cause; it is a diagnosis when no cause is known.

Specifically, Wyeth argues that Cheek has failed to rule out IPAH as a cause of her PAH, thereby disqualifying her from bringing this case. Although there are other conditions that can secondarily cause PAH that are not referenced in Section I.46, these causes do not include IPAH.[53] By definition, the term IPAH "corresponds to sporadic disease in which there is neither a family history of PAH nor an identified risk factor."[54] Again, IPAH is not a cause of PAH but is rather a label used to describe PAH with an unknown cause. As previously discussed, a diagnosis of IPAH is logically and medically impossible when a patient presents with a history of diet drug exposure.[55] Additionally, although not required by the NSA definition of PPH, Plaintiff's experts have, in fact,

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[52] PTO 2383 at ¶ 3 (emphasis added).
[53] Other conditions include HIV Infection, Schistosomiasis, and Chronic Hemolytic Anemia. Simonneau, *supra* note 12, S45 (Table 2). If Plaintiff had any of these conditions, her blood tests would have indicated so. *But see* MUSC, 32-33 (Indicating that Plaintiff's lab results were normal and that she tested negative for HIV).
[54] Simonneau, *supra* note 12, S44.
[55] *See supra* pp. 5-6.

considered the possibility of a diagnosis of IPAH, and, based on their interpretations of scientifically reliable sources that satisfy the *Daubert* standards, they have concluded that IPAH would be an improper diagnosis of Ms. Cheek's PAH.[56]

Wyeth's request to enjoin Cheek's case pursuant to PTO 2383 is a feeble attempt to amend the terms of the NSA in its favor, supplementing the PPH diagnostic criteria with requirements that were never negotiated or agreed to. This fact is apparent when considering the illogical reasoning Wyeth relies on when it suggests that all conditions known to cause pulmonary hypertension must be ruled out before a plaintiff can pursue a claim, including any and all *unknown or idiopathic* causes. Such a proposition is patently absurd.

Thus, as Cheek has satisfied the three-part test established in Section I.46, and in light of the original intent of the NSA, Cheek respectfully requests that this Court deny Wyeth's motion to enjoin Plaintiff's case.

VI. CONCLUSION

For the foregoing reasons, we respectfully submit that the Court should deny with prejudice Defendant Wyeth's Motion to Exclude Expert Testimony and Enjoin Plaintiff Cheek's Case Pursuant to Pretrial Order No. 2383.

Respectfully submitted this 8th day of August, 2012.

s/ Elizabeth M. Burke
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Certificate of Service

I hereby certify that a true and correct copy of the foregoing Plaintiff Cheek's Response in Opposition to Defendants Wyeth's Motion to Exclude Expert Testimony and Enjoin Plaintiff Cheek's Case Pursuant to Pretrial Order No. 2383 in Jamie D. Cheek v. Weyth, f/k/a American Home Products Corporation, et al, Case No. 11-20001 in IN RE: DIET DRUGS (Phentermine/Fenfluramine/Dexfenfluramine) PRODUCTS LIABILITY LITIGATION; MDL Docket No. 1203, was filed electronically this 8th day of August, 2012, and is available for viewing and downloading from the court's CM/ECF System. Furthermore, a hardcopy has been served on the parties listed below via UPS Next Day Air Service.

This 8th day of August 2012.

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